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## FEE TRANSMITTAL

Complete if known

Application Number: 09/359,181

Filing Date: July 22, 1999

First Named Inventor: Grassy, et al.

Group Art Unit: 1631

Examiner Name: Lori A. Chow

Total Amt. of Payment: (1)+(2)+(3)= \$0

Attorney Docket Number: 1028-1

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METHOD OF PAYMENT (check one)		FEE CALCULATION (continued)																																							
<p>1. The Commissioner is hereby authorized to:</p> <p><input type="checkbox"/> Charge indicated fees</p> <p><input checked="" type="checkbox"/> Charge additional fees</p> <p><input checked="" type="checkbox"/> Credit overpayments</p> <p>to the account of DANN, DORFMAN, HERRELL &amp; SKILLMAN</p> <p>Deposit Account Number <u>04-1406</u></p> <p>2. Payment enclosed:</p> <p>Check in the amount of <u>\$0</u></p>		<p><b>ADDITIONAL FEES</b></p> <table><thead><tr><th>Fee Description</th><th>Fee Paid</th></tr></thead><tbody><tr><td>Surcharge-late filing fee or oath</td><td></td></tr><tr><td>Surcharge - late provisional filing fee or cover sheet</td><td></td></tr><tr><td>Extension for response within first month</td><td></td></tr><tr><td>Extension for response within second month</td><td></td></tr><tr><td>Extension for response within third month</td><td></td></tr><tr><td>Extension for response within fourth month</td><td></td></tr><tr><td>Notice of Appeal</td><td></td></tr><tr><td>Filing a brief in support of an appeal</td><td></td></tr><tr><td>Request for oral hearing</td><td></td></tr><tr><td>Petition to revive unavoidably abandoned application</td><td></td></tr><tr><td>Petition to revive unintentionally abandoned application</td><td></td></tr><tr><td>Issue fee</td><td></td></tr><tr><td>Petitions to the Commissioner</td><td></td></tr><tr><td>Petitions related to provisional applications</td><td></td></tr><tr><td>Submission of Information Disclosure Stmt</td><td></td></tr><tr><td>Recording each patent assignment per property</td><td></td></tr><tr><td>Other fee (specify) <u>Advance Order (10 copies)</u></td><td></td></tr><tr><td>Other fee (specify)</td><td></td></tr></tbody></table> <p><b>SUBTOTAL (3)</b> <u>\$0</u></p>		Fee Description	Fee Paid	Surcharge-late filing fee or oath		Surcharge - late provisional filing fee or cover sheet		Extension for response within first month		Extension for response within second month		Extension for response within third month		Extension for response within fourth month		Notice of Appeal		Filing a brief in support of an appeal		Request for oral hearing		Petition to revive unavoidably abandoned application		Petition to revive unintentionally abandoned application		Issue fee		Petitions to the Commissioner		Petitions related to provisional applications		Submission of Information Disclosure Stmt		Recording each patent assignment per property		Other fee (specify) <u>Advance Order (10 copies)</u>		Other fee (specify)	
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Submitted By  
Typed or

Printed Name Donald R. Piper, Jr.

Reg. Number 29,337

Deposit Account User ID

Signature

Date January 17, 2003

04-1406



**EXPEDITED PROCESSING REQUESTED:  
RESPONSE AFTER FINAL**

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JAN 24 2003  
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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re the Application of

Gerard Grassy et al.

Serial No. 09/359,181

Filed: July 11, 1999

For: Computer-Aided Method for  
the Provision,  
Identification, and  
Description of Molecules  
Capable of Exhibiting a  
Desired Behavior, More  
Particularly in the  
Pharmaceutical Sector, and  
Molecules Obtained by Said  
Method

Examiner: Lori A. Clow

Group Art Unit: 1681

Response to Paper No. 26

Our File No. 1028-1

**CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)**

I hereby certify that this correspondence is being  
deposited on January 17, 2003 with the United States Postal  
Service as first class mail in an envelope properly addressed  
to COMMISSIONER OF PATENTS AND TRADEMARKS, Washington, D.C.  
20231.

1/17/2003  
Date

Robin Delan  
Robin Delan

**REQUEST FOR RECONSIDERATION UNDER 37 C.F.R. §1.116**

The Official Action issued November 18, 2002 has been  
carefully reviewed. In view of the following remarks and  
evidence, favorable reconsideration and allowance of this  
application is respectfully requested.

At page 1 of the Official Action, the Examiner has  
maintained the rejection of claims 1, 4, 5, 8-10, and 18-20  
under 35 U.S.C. §112, first paragraph as allegedly containing

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file  
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Serial No. 09/359,181  
Filed: July 22, 1999

Examiner: L. Clow  
Group Art Unit: 1631

subject matter which was not described in the specification in such a way as to enable one of skill in the art to make and/or use the invention. Specifically, the Examiner argues that the phrases "building", "selecting", and "modeling" without concrete active steps to eliminate undue experimentation do not enable the instant invention. This issue has been addressed previously by Applicants, most recently with the arguments filed with the response filed August 26, 2002. Previously, Applicants asserted and continue to maintain that the "building", "selecting", and "modeling" steps are all adequately described in the specification.

In response to the arguments filed August 26, 2002, the Examiner has simply restated the reasons for rejection made in the May 21, 2002 Official Action and brought the description of the TSAR software in to question. Specifically, the Examiner states that "nowhere in the specification is one appraised of the framework of this particular software such that one of skill in the art could ascertain specific calculations." Applicants disagree with the Examiner's requirement for a description of the framework of the software. Clearly, one of skill in the art at the time the instant application was filed would be capable of utilizing the **commercially** available TSAR software with reference guide. If needed, additional assistance and information could have been obtained from the distributing company Oxford Molecular Group (currently TSAR is distributed by Accelrys, Inc, San Diego, CA). Plainly, one of skill in the art would be capable of utilizing the software to determine molecular descriptors without undue experimentation and therefore the specification is enabling.

Additionally, the Examiner asserts that the citing of the TSAR software is unclear because "TSAR could refer to any of various versions of this software available." Again,

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Applicants disagree with the Examiner's position. Indeed, at page 30, line 30 of the specification, TSAR version 2.31 available from the Oxford Molecular Group is specifically referenced. Applicants also submit, however, that any version of TSAR from the original version 1.0 to the current version 3.3 would be suitable for the instant invention. The same formulas and algorithms are implemented in each version and would therefore provide the same values for the descriptors of a given molecule.

The Examiner also questions which "parameters are chosen in order to generate the descriptors" and whether the parameters are user-defined or set as default within the software. Applicants respectfully point out to the Examiner that molecular descriptors are not based on user-defined parameters. As a skilled artisan would appreciate, molecular descriptors are standard entities described in detail in standard works. Select pages of the recent publication "Handbook of Molecular Descriptors" (R. Todeschini and V. Consonni (2000) Wiley-VCH; Exhibit A) are enclosed. Specifically, the provided pages illustrate two descriptors, the Balban indices (p. 21-23) and Kier shape descriptors (p. 248-250), which were standard descriptors at the time the instant the instant application was filed (note the references cited on pages 23 and 250). Just as there is only one way to calculate the molecular weight of a given molecule, there is only one way to calculate its Balban index or Kier shape descriptor or any of the hundreds of other descriptors available. To this end, Applicants have also enclosed select pages, notably pages 1-13 and 1-18 to 1-22, from the "TSAR Reference Guide" (Exhibit B) which describe the Balban indices and Kier shape descriptors in the same manner as the "Handbook of Molecular Descriptors." Additionally, Applicants point out that other commercially available software such as any version

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of MolConnZ (EduSoft, USA) capable of performing molecular descriptor calculations uses these standard descriptors (a list of software is provided in Appendix C of the "Handbook of Molecular Descriptors"). A skilled artisan would appreciate that any of these software packages capable of computing molecular descriptors could be utilized to perform the molecular modeling step of the invention and generate descriptors in a reproducible manner.

At page 4 of the November 18, 2002 Official Action, the Examiner also states that "without disclosure of the steps provided by said software...to build, select, or model, one of skill in the art would not know how to practice the invention." From this statement, the Examiner seems to suggest that the software package used to perform the molecular modeling is also used to perform the building of the combinatorial library and the selection of candidate molecules. Applicants respectfully submit that the Examiner is incorrect in this assessment. The TSAR software and other software capable of computing molecular descriptors are implemented only in the molecular modeling step of the instant invention. The arguments set forth hereinabove demonstrate how the description enables this step. The Examiner is referred to page 13, line 23 to page 15, line 22 and page 33, line 19 to page 34, line 6 for a detailed description of steps involved in the building of a combinatorial library. Moreover, software specific to assisting in the creation of the combinatorial explosion such as Combex and Legion are also provided. As with the TSAR software, the software for the creation of the combinatorial explosion would be easily accessed and employed by one of skill in the art. The Examiner is also referred to page 34, lines 7 to 17 for a detailed description of an example for the selection of

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candidate molecules. All steps of the present invention are adequately described and enabled.

As further evidence that there is no ambiguity or lack of detail in the description of the invention of the instant application, Applicants mention that a similar description was published soon after the filing of this application (Grassy, G. et al. (1998) "Computer-assisted rational design of immunosuppressive compounds," Nature Biotechnology, 16:748-752; submitted in Information Disclosure Statement of May 3, 2002). Nature Biotechnology is a journal that is well known for its high standards of scientific quality and accuracy and, notably, no objection of the manuscript for inadequate description was made by a review panel of independent referees, i.e. ones of skill in the art.

Applicants contend the foregoing remarks and evidence clearly demonstrate that the description in the specification is enabling and that no undue experimentation would be required to practice the invention. Thus, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

It is respectfully requested that the foregoing remarks and evidence presented herewith be entered in this application, since it is believed they clearly place the pending claims in condition for allowance.

The above listed rejection constitutes the entirety of the issues raised in the Official Action dated November 18, 2002. In light of the foregoing remarks and evidence, Applicants believe that the claims as they stand are in condition for ready allowance.

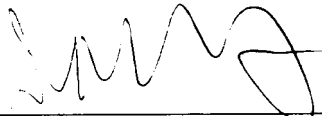
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In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number give below.

Respectfully submitted,

DANN, DORFMAN, HERRELL AND SKILLMAN  
A Professional Corporation



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Donald R. Piper, Jr.  
Registration No. 29,337

Telephone: 215-563-4100

-Enclosures: Exhibits A and B